REMARKS

1. Restriction/Unity

The Examiner maintains the restriction to group II. We realize that groups I (cp. claims 80-81) and III (cp. claims 82-83) would not be rejoined unless and until a group II claim is deemed allowable. However, we have traversed the prior art rejection of the group II claims, and if that traversal is deemed persuasive, the restriction must be reconsidered.

The Examiner is of the position that PCT unity practice would allow rejoinder of only the first recited method of use. That is incorrect. PCT Rule 13.2 says that unity is fulfilled for a "group of inventions" when there is a sufficient technical relationship connecting the inventions. It does not limit the size of the group.

Moreover, even if the Examiner were correct, group I defines a method of making the T cells of group II. The method of use is set forth in group III.

The Examiner's attention is also directed to rejoinder practice under MPEP 821.04. This provides for rejoinder of all "withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim", regardless of the number of different processes of making and/or using the patentable product which are contemplated. Claims 80-83 satisfy the dependency requirement of MPEP 821.04.

2. Definiteness Issues

2.1. Claim 40 has been rewritten independent of claim 1.

2.2. The Examiner criticizes the use of "continuous" in claim 1 even though he acknowledges its definition on page 9. Claim 1 has been cancelled. We have amended claim 40 to substitute the actual definition (expected or actual "life span

of at least 40 PD") for the term.

2.3. We have corrected the Markush group language of claim 47 by replacing 47 with new claim 78.

2.4. The meaning of "attenuation" (claim 48) is that explained by page 38, lines 21-25:

> The T-cells are preferably attenuated prior to administration in order to ensure that the cells are not able to divide further. Such attenuation may suitably be accomplished by x-ray or UV radiation or by addition of cell poisons.

We have replaced claim 49 with new claim 79, which states that the "cells are incapable of further cell division".

2.5. Claims 44-48 have been replaced with new claims 75-79, which replace "vaccine" with --immunological composition--.

3. Prior Art Issues

3.1 The Examiner says that because the term "continuous" is indefinite, it was given no weight for purposes of distinguishing the prior art. That is improper. MPEP 2173.06 says, "All words in a claim must be considered in judging the patentability of a claim against the prior art... The fact that terms may be indefinite does not make the claim obvious over the prior art".

The Examiner is permitted to state that the claim is subject to more than one interpretation and to reject the claim on the basis of a specified interpretation. The Examiner could fairly interpret "continuous" as equivalent to 40 PD, but cannot simply ignore the term.

3.2. The Examiner asserts that "continuous" is defined at page 9 as a "half-life" of at least 40 P.D. The Examiner argues that, so defined, the cells do not exceed the Hayflick limit and

hence are no more "continuous" than run-of-the-mill mammalian cell culture.

The Hayflick limit is first mentioned at page 1, line 32 to page 2, line 12. Contrary to the Examiner's position, applicant discloses that the Hayflick limit is 23 PD. The Examiner does not cite any literature in support of a higher Hayflick limit.

We have replaced the present recitation of "continuous", with an explicit recitation in terms of PD. We have also added dependent claims (85-88), reciting higher PD values. There is support for at least 60 PD (P9, L36), 100 PD (P10, L1), 150 PD (P10, L2) and 200 PD (P10, L2).

Reviewing the Examples, it can be seen that applicants achieved proliferation at least beyond 150 PD.

3.3. Anticipation by Riddell (ref. AB) (claims 40, 43-46, 48)

The Examiner asserts that Riddell's cells are "human antigen-specific, cytotoxic T cells grown by stimulation with IL-2 and anti-CD3".

Riddell says that he expanded T-cells in the range of 500-3000 fold expansion in 8 to 14 days. Col. 9, lines 38-40. That corresponds to a change of 9 to 12 PD. However, it is unclear how many divisions the cells in question had already under gone.

At col. 9, lines 62-64, he speaks of expanding individual T cell clones to greater than 10^9 cells. 10^9 cells would be equivalent to about 30 PD. That is still well <u>below</u> 40 PD (although <u>above</u> the <u>disclosed</u> Hayflick limit).

Plainly, Riddell does not anticipate.

3.4. Anticipation by Haberman (ref. AA) (claims 40, 43-46)

At col. 19, lines 44-50, Haberman speaks of expansion to 10^7-10^8 lymphocytes. That is poorer performance than Riddell's.

3.5. Anticipation by Liu (ref. AE) (claims 40, 44-46, 48)

The Examiner asserts that the protocol on page 12 is indistinguishable from applicants' "all inclusive disclosure". At most there was a 620-fold increase in T cell numbers (P36, L7-12), which is a PD change of slightly more than 8. This does not seem impressive.

The method of Liu describes cells (MNC) isolated from a blood sample. The isolated cells comprise cells specific for the viral antigen, however the specific cells are not necessarily in vivo activated. This step is important, since the present invention only describes in vivo (disease associated antigen) activated T cells. Furthermore the cells are cultured in the presence of antigen presenting cells and viral antigen, which we are not reciting in the present claims.

3.6. Anticipation by Kaltoft (ref. AU) (claims 40, 44)

The Examiner implicitly recognized that Kaltoft did not anticipate claim 43. The limitation of claim 43 (cytotoxic T cells) has been incorporated into claim 40. The reference discloses expansion of inflammatory T cells.

3.7. Anticipation by Boel (USP 5,877,017) (claims 40, 43-46)

The specification says nothing about expansion of cells beyond the Hayflick limit.

3.8. Anticipation by Smith (US 2002/0034819) (claims 40, 43, 44)

Smith speaks of secondary culture expansion of cells 2000-fold (paragraph 0031), which is a PD change of 11. It is unclear what is the final PD achieved. However, Smith suggests in paragraph 36 that the improvement is 10-fold relative to static culture. If the latter were to the Hayflick limit (23), a 10-

fold change would still result in a total PD of not more than 27.

Respectfully submitted,

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